General

Guideline Title

Orthostatic hypotension.

Bibliographic Source(s)

Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W, Tassinari M. Orthostatic hypotension. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 469-75. [53 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W, Tassinari M. EFNS guidelines on the diagnosis and management of orthostatic hypotension. Eur J Neurol 2006 Sep;13(9):930-6.

Recommendations

Major Recommendations

The levels of evidence (Class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good Practice Point [GPP]) are defined at the end of the "Major Recommendations" field.

Diagnostic Strategies

Protocol

1. Orthostatic testing should take place in a quiet room, at a temperature between 20º C and 24º C. The patient should rest while supine for ideally 5 minutes before head-up tilt testing (HUT) is started. Emptying the bladder before testing is recommended.
2. Passive HUT to an angle between 60º and 80º for 3 minutes is recommended for the diagnosis of orthostatic hypotension (OH).
3. HUT is considered positive if systolic blood pressure (BP) falls below 20 mm Hg and diastolic BP below 10 mm Hg of baseline. If symptoms occur, the patient should be tilted back to the supine position immediately.
4. Measurement of plasma noradrenaline levels while supine and upright may be of value.
5. In contrast with cardiologic guidelines, pharmacological provocation with sublingual nitroglycerine or intravenous isoproterenol is not recommended to diagnose OH as it reduces sensitivity and will result in false positive outcomes.
6. Combination of HUT and physiological measures, such as lower body negative pressure application, as used in neurally mediated syncope, is not recommended for diagnosis of OH.

HUT is a safe procedure for the diagnosis of OH. However, as syncope and arrhythmias have been described, the investigating staff should be

adequately trained to recognize such problems. Resuscitation equipment and a team experienced in cardiac life support should be available at short notice (GPP).

Level C Recommendations

- Structured history taking
- Detailed physical examination
- 12-lead electrocardiogram (ECG) recording
- Routine laboratory testing
- BP measurements while supine and upright
- Cardiologic referral, if heart disease or abnormal ECG is present or suspected
- Active standing or HUT, ideally with continuous assessment of BP and heart rate (HR) for 3 min
- Further autonomic nervous system (ANS) screening tests, with other appropriate investigations, depending on the possible aetiology of the underlying disorder (Mathias, 2003)

Management

The following recommendations are mainly a result of panel consensus and qualified as GPP.

Elevated environmental temperatures, a hot bath or shower, and sauna should be avoided as they cause venous pooling. Prolonged recumbence during daytime and sudden head up postural change, particularly in the morning, when BP may be lowered by nocturnal polyuria, should be avoided. Post-prandial hypotension may increase OH (vasodilatation in splanchnic vessels). Large meals, especially carbohydrate-rich, and alcohol should be avoided. A carefully controlled and individualized exercise training (swimming, aerobics, and, if possible, cycling and walking) often improves OH.

Supine Hypertension

Supine hypertension may be a problem, resulting from medication and/or being part of the disease. Therefore, 24 hour measurement of BP is best before and if needed after starting a new therapy. Patients may self-monitor BP daily at about the same time, and when they experience symptoms. Pressor medications should be avoided after 6 pm and the bed head elevated (20–30 cm). On occasion, short acting antihypertensive drugs may be considered (e.g., nitroglycerine sublingual).

Non-Pharmacological Treatment

Avoidance of factors that may induce OH is recommended first line, particularly in mild forms. Educating the patients and carers on the mechanisms of OH is important. The next step includes a range of non-pharmacological strategies.

Patients should be advised to move to head-up position slowly, sit on the edge of the bed for some minutes after recumbence, and activate calf muscles while supine. Physical counter manoeuvres can be applied immediately at the onset of pre-syncopal symptoms. They need to be explained and trained individually. In case of motor disabilities and compromised balance, as in the cerebellar forms of multiple system atrophy (MSA), programmes with appropriate aids have to be developed. Leg crossing with tension of the thigh, buttock and calf muscles (party position), bending over forward to reduce the orthostatic difference between the heart and brain and compress the splanchnic vessels by increasing abdominal pressure, squatting to reduce blood pooling are effective in temporarily reducing OH. Not all patients can perform these manoeuvres and sitting or lying down, and using a cane that can be folded into a tripod chair, are useful. Elastic stockings and abdominal compression bands reduce venous pooling and have been shown effective in small studies. Sleeping with elevation of the head-end of the bed (20 to 30 cm), particularly in combination with low dose fludrocortisone, improves OH.

To compensate for renal salt loss a liberal intake of salt, at least 8 g (150 mmol) of sodium chloride daily, if needed as salt tablets (starting dose 500 mg three times a day [t.i.d.]), are recommended. Water repletion (2 to 2.5 l/day) is important, while 500 mL of water is effective in rising BP immediately.

Cardiac pacing is not recommended in neurogenic OH.

Pharmacological Treatment

Fludrocortisone

Level C Recommendations

- Fludrocortisone as first line drug monotherapy of OH (0.1 to 0.2 mg per day)

- Full benefit requires a high dietary salt and adequate fluid intake
- Combination of a high salt diet, head-up tilt sleeping (20 to 30 cm) and a low dose of fludrocortisone (0.1 to 0.2 mg) is an effective means of improving OH (van Lieshout, ten Harkel, & Wieling, 2000)

Mild dependent oedema can be expected and fludrocortisone should be used with caution in patients with a low serum albumin. Higher doses of fludrocortisone can result in fluid overload and congestive heart failure, severe supine hypertension and hypokalaemia (Schatz, Miller, & Frame, 1976). To prevent hypokalaemia, food rich in potassium such as fruits, vegetables, poultry, fish and meat is advisable. Headache may occur, especially while supine.

Midodrine

Level A Recommendations

- Midodrine is recommended for mono- or combined therapy (e.g., with fludrocortisone).
- Initial dosage is 2.5 mg orally two to three times daily increasing gradually up to 10 mg t.i.d.
- Supine hypertension is a common (25%) adverse effect and may be severe. The last dose should be administered at least 4 hours before going to sleep and BP should be monitored.
- Adverse effects are piloerection (goose bumps, 13%), scalp or general pruritus (10% and 2%), scalp or general paraesthesia (9% each), urinary retention (6%), and chills (5%).

Some patients worsen on midodrine, maybe due to adrenoceptor desensitization (Kaufmann et al., 1988). It should be administered with caution in patients with hepatic dysfunction and is contraindicated in severe heart disease, acute renal failure, urinary retention, phaeochromocytoma, and thyrotoxicosis (McClellan, Wiseman, & Wilde, 1998).

Dihydroxyphenylserine (DOPS)

Level A Recommendations

In a dosage between 200 and 400 mg per day L-DOPS reduces OH. It is the only effective treatment of dopamine beta-hydroxylase deficiency. In all studies reviewed, no major side effects were reported. Future studies will have to investigate which patient groups benefit most from this drug.

Octreotide

Level C Recommendations

Subcutaneous doses of 25 to 150 μg 30 minutes before a meal may be used to reduce postprandial OH. It does not increase supine hypertension. Nausea and abdominal cramps may occur.

Other Treatment Options

For the drugs listed below there is no clear evidence for use in OH. Many are recommended as GPP and warrant future studies.

Ephedrine that acts on alpha- and beta-adrenergic receptors is recommended by the authors, as it reduces OH in many patients, particularly with central lesions like MSA (15 mg t.i.d.). Yohimbine, an alpha-2-adrenoceptor antagonist with central and peripheral effects, has been used in refractory OH (6 mg daily) (Class III).

Dihydroergotamine (DHE), a direct alpha-adrenoceptor agonist stimulating constriction of venous capacity vessels, has shown some benefit and may be used in severe OH (3 to 5 mg t.i.d. oral) (Level C, Class III, Class IV).

Desmopressin, a vasopressin analogue, acts on renal tubular vasopressin-2 receptors, diminishing nocturnal polyuria, and may be applied as nasal spray (10 to 40 μg) or orally (100 to 400 μg) at night (Class IV).

Erythropoietin is recommended in anaemic patients, particularly in familial amyloidosis. Indomethacin, a prostaglandin synthetase inhibitor, has been used in severe OH (75 to 150 mg/day) (Class IV, Class III).

Pyridostigmine may be effective in the treatment of OH through potentiation of sympathetic cholinergic ganglionic transmission, leading to increased vascular tone in the upright position. In a double-blind, randomized, four-way crossover study the acute effects of 60 mg pyridostigmine bromide on supine and upright BP were tested against midodrine and placebo. Pyridostigmine significantly improved standing BP without worsening supine hypertension. However, further studies on the long-term efficacy and on possible adverse effects have to be performed before this treatment can be evaluated.

Summary

- OH is defined as fall in BP within 3 minutes of active standing or HUT.
- The key to managing OH is individually tailored therapy. The goal of treatment is to improve the patient's functional capacity and quality of life, preventing injury, rather than to achieve a target BP.
- Management of patients with OH consists of education, advice and training on various factors that influence blood pressure, and special aspects that have to be avoided (foods, habits, positions and drugs).
- Physical measures include leg crossing, squatting, elastic abdominal binders and stockings, and careful exercise (GPP).
- Increased water (2 to 2.5 l/day) and salt ingestion (>8 g or 150 mmol/day) effectively improve OH.
- Fludrocortisone is a valuable starter drug (0.1 to 0.2 mg day, Level C). Second-line drugs include sympathomimetics, such as midodrine (start with 2.5 mg twice daily (b.i.d.) and increase to 10 mg t.i.d., Level A) or ephedrine (15 mg t.i.d., GPP). DOPS (200 to 400 mg daily, Level A) reduces OH with only minor side effects. It is an effective treatment in dopamine beta-hydroxylase deficiency.
- Supine hypertension has to be considered.
- Individual testing with a series of drugs, based on the risk of side effects, pharmacological interactions and probability of response in the individual patient, may be considered when the measures shown here should not be satisfactory.

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming

class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point Where there was a lack of evidence but consensus was clear, the task force has stated their opinion as Good Practice Points.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Orthostatic (postural) hypotension

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Intended Users

Physicians

Guideline Objective(s)

To provide physicians with evidence-based guidelines for clinical and laboratory diagnostic workup and therapeutic management of orthostatic hypotension (OH)

Target Population

Patients with orthostatic hypotension (OH)

Interventions and Practices Considered

Diagnosis/Evaluation

1. Structured history taking
2. Detailed physical and neurological examination
3. 12-lead electrocardiogram (ECG)
4. Routine laboratory testing
5. Blood pressure (BP) testing in supine and upright positions
6. Cardiologic referral if indicated
7. Active standing or head-up tilt (HUT) with assessment of BP and heart rate for 3 min
8. Autonomic nervous system screening tests and other investigations depending on etiology of the underlying disorder

Management/Treatment

1. Individualized therapy
2. Patient education about mechanisms of orthostatic hypertension and various factors that influence BP
3. Carefully controlled and individualized exercise training (swimming, aerobics, cycling, and walking)
4. Self-monitoring of blood pressure (BP)
5. Physical measures including leg crossing, squatting, elastic stockings and abdominal compression bands
6. Increased water and salt ingestion
7. Pharmacological treatment including fludrocortisone, midodrine or ephedrine, dihydroxyphenylserine (DOPS), subcutaneous octreotide
8. Management of supine hypertension if needed

Note: The following interventions were considered but not recommended: pharmacological provocation during HUT with sublingual nitroglycerine or intravenous isoproterenol to diagnose orthostatic hypertension (OH); combination of HUT and physiological measures, such as lower body negative pressure application to diagnose OH; cardiac pacing; certain medications such as yohimbine, dihydroergotamine, desmopressin, and others may be used in selected cases.

Major Outcomes Considered

- Effectiveness of diagnosis/evaluation
- Effectiveness of treatment
- Functional capacity and quality of life
- Side effects of medications

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Electronic search strategies used the following databases: Cochrane library, PubMed, Medline and various internet search routines, for English publications. Key search terms included: 'orthostatic hypotension', 'syncope', 'hypotension' and 'therapy', 'treatment', and 'diagnosis', and first year availability of each referenced literature database until October 2009. References classified by evidence levels were selected by one individual and checked by another investigator.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Where there was a lack of evidence but consensus was clear, the task force has stated their opinion as Good Practice Points (GPPs).

Rating Scheme for the Strength of the Recommendations

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point Where there was a lack of evidence but consensus was clear, the task force has stated their opinion as Good Practice Points.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

References Supporting the Recommendations

Kaufmann H, Brannan T, Krakoff L, Yahr MD, Mandeli J. Treatment of orthostatic hypotension due to autonomic failure with a peripheral alpha-adrenergic agonist (midodrine). Neurology. 1988 Jun;38(6):951-6. PubMed

Mathias CJ. Autonomic diseases: clinical features and laboratory evaluation. J Neurol Neurosurg Psychiatry. 2003 Sep;74(Suppl 3):iii31-41. [27 references] PubMed

McClellan KJ, Wiseman LR, Wilde MI. Midodrine. A review of its therapeutic use in the management of orthostatic hypotension. Drugs Aging. 1998 Jan;12(1):76-86. [32 references] PubMed

Schatz IJ, Miller MJ, Frame B. Corticosteroids in the management of orthostatic hypotension. Cardiology. 1976;61(Suppl 1):280-9. PubMed

van Lieshout JJ, ten Harkel AD, Wieling W. Fludrocortisone and sleeping in the head-up position limit the postural decrease in cardiac output in autonomic failure. Clin Auton Res. 2000 Feb;10(1):35-42. PubMed

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of orthostatic hypotension to improve patient's functional capacity and quality of life

Potential Harms

Diagnostic Procedures

Head-up tilt (HUT) is a safe procedure for the diagnosis of orthostatic hypertension (OH). However, as syncope and arrhythmias have been described, the investigating staff should be adequately trained to recognize such problems. Resuscitation equipment and a team experienced in cardiac life support should be available at short notice.

Adverse Effects of Medications

- *Fludrocortisone*. Mild dependent oedema can be expected and fludrocortisone should be used with caution in patients with a low serum albumin. Higher doses of fludrocortisone can result in fluid overload and congestive heart failure, severe supine hypertension and hypokalaemia. To prevent hypokalaemia, food rich in potassium such as fruits, vegetables, poultry, fish and meat is advisable. Headache may occur, especially while supine.
- *Ephedrine*. Common adverse effects of *sympathomimetics* with a central action, such as ephedrine, are tachycardia, anxiety, restlessness, insomnia and tremor. Dry mouth, impaired circulation to the extremities, supine hypertension, and cardiac arrhythmias may occur.
- *Midodrine*. Supine hypertension is a common (25%) adverse effect of midodrine and may be severe. The last dose should be administered at least 4 hours before going to sleep and blood pressure should be monitored. Adverse effects are piloerection (goose bumps, 13%), scalp or general pruritus (10% and 2%), scalp or general paraesthesia (9% each), urinary retention (6%), and chills (5%). Some patients worsen on midodrine, maybe due to adrenoceptor desensitization. It should be administered with caution in patients with hepatic dysfunction.
- *Octreotide*. Nausea and abdominal cramps may occur.

Contraindications

Contraindications

Midodrine is contraindicated in severe heart disease, acute renal failure, urinary retention, phaeochromocytoma, and thyrotoxicosis.

Qualifying Statements

Qualifying Statements

Qualifying Statements

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.
Tests to investigate orthostatic hypotension are considered here and not general investigations of the autonomic nervous system. A limitation is a paucity of randomized and blinded studies. The wide variation of test methods, protocols and equipment in autonomic laboratories make comparison of results difficult.

Implementation of the Guideline

Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W, Tassinari M. Orthostatic hypotension. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 469-75. [53 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Sep (revised 2011)

Guideline Developer(s)

European Academy of Neurology - Medical Specialty Society

Source(s) of Funding

The present guidelines were developed without external financial support.

Guideline Committee

European Federation of Neurological Societies Task Force on Orthostatic Hypotension

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Financial Disclosures/Conflicts of Interest

None of the authors reports conflicting interests.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W, Tassinari M. EFNS guidelines on the diagnosis and management of orthostatic hypotension. Eur J Neurol 2006 Sep;13(9):930-6.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies (EFNS) Web site .

Availability of Companion Documents

The following is available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on April 10, 2007. The information was verified by the guideline developer on May 15, 2007. This summary was updated by ECRI Institute on July 9, 2007, following the FDA advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on December 7, 2007, following the U.S. Food and Drug Administration advisory on Desmopressin Acetate. This summary was updated by ECRI Institute on March 21, 2008 following the FDA advisory on Erythropoiesis Stimulating Agents. This summary was updated by ECRI Institute on August 15, 2008 following the U.S. Food and Drug Administration advisory on Erythropoiesis Stimulating Agents (ESAs). This summary was updated by ECRI Institute on April 1, 2010 following the U.S. Food and Drug Administration advisory on Erythropoiesis-Stimulating Agents (ESAs). This NGC summary was updated by ECRI Institute on February 20, 2012. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

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